Figure 1. Amino acid sequence alignment in human IgG isotypes and their variants.

Human IgG Isotype	Amino Acid Position				
	228.....234	235	236	237.....330	331
G1 (SEQ ID NO:26)	Pro.....Leu	Leu	Gly	Gly.....Ala	Pro
G2 (SEQ ID NO:27)	Pro.....Val	Ala	.....	Gly.....Ala	Pro
G4 (SEQ ID NO:28)	Ser.....Phe	Leu	Gly	Gly.....Ser	Ser
G1 variant (SEQ ID NO:22)	Pro.....***Val***	***Ala***	Gly	Gly.....Ala	***Ser***
G2 variant (SEQ ID NO:18)	Pro.....Val	Ala	.....	Gly.....Ala	***Ser***
G4 variant (SEQ ID NO:20)	***Pro***.....Phe	***Ala***	Gly	Gly.....Ser	Ser

Figure 2A. DNA and deduced amino acid sequences of HuEPO-L-vFc$_{\gamma 2}$

DNA Sequence SEQ ID NO: 17

Amino Acid Sequence SEQ ID NO: 18

```
aag ctt ggc gcg gag atg ggg gtg cac gaa tgt cct gcc tgg ctg tgg ctt ctc ctg tcc  60
HindIII              M   G   V   H   E   C   P   A   W   L   W   L   L   L   S
                    -27                                 -20
ctg ctg tcg ctc cct ctg ggc ctc cca gtc ctg ggc gcc cca cca cgc ctc atc tgt gac  120
 L   L   S   L   P   L   G   L   P   V   L   G   A   P   P   R   L   I   C   D
         -10                                     -1   1
agc cga gtc ctg gag agg tac ctc ttg gag gcc aag gag gcc gag aat atc acg acg ggc  180
 S   R   V   L   E   R   Y   L   L   E   A   K   E   A   E   N   I   T   T   G
     10                                      20
tgt gct gaa cac tgc agc ttg aat gag aat atc act gtc cca gac acc aaa gtt aat ttc  240
 C   A   E   H   C   S   L   N   E   N   I   T   V   P   D   T   K   V   N   F
     30                                      40
tat gcc tgg aag agg atg gag gtc ggg cag cag gcc gta gaa gtc tgg cag ggc ctg gcc  300
 Y   A   W   K   R   M   E   V   G   Q   Q   A   V   E   V   W   Q   G   L   A
     50                                      60
ctg ctg tcg gaa gct gtc ctg cgg ggc cag gcc ctg ttg gtc aac tct tcc cag ccg tgg  360
 L   L   S   E   A   V   L   R   G   Q   A   L   L   V   N   S   S   Q   P   W
     70                                      80
gag ccc ctg cag ctg cat gtg gat aaa gcc gtc agt ggc ctt cgc agc ctc acc act ctg  420
 E   P   L   Q   L   H   V   D   K   A   V   S   G   L   R   S   L   T   T   L
     90                                      100
ctt cgg gct ctg gga gcc cag aag gaa gcc atc tcc cct cca gat gcg gcc tca gct gct  480
 L   R   A   L   G   A   Q   K   E   A   I   S   P   P   D   A   A   S   A   A
    110                                     120
cca ctc cga aca atc act gct gac act ttc cgc aaa ctc ttc cga gtc tac tcc aat ttc  540
 P   L   R   T   I   T   A   D   T   F   R   K   L   F   R   V   Y   S   N   F
    130                                     140
ctc cgg gga aag ctg aag ctg tac aca ggg gag gcc tgc agg aca ggg gac gga tcc ggt  600
 L   R   G   K   L   K   L   Y   T   G   E   A   C   R   T   G   D   G   S   G
    150                                     160
ggc ggt tcc ggt gga ggc gga agc ggc ggt gga gga tca gag cgc aaa tgt tgt gtc gag  660
 G   G   S   G   G   G   G   S   G   G   G   G   S   E   R   K   C   C   V   E
    170                                     180
tgc cca ccg tgc cca gca cca cct gtg gca gga ccg tca gtc ttc ctc ttc ccc cca aaa  720
 C   P   P   C   P   A   P   P   V   A   G   P   S   V   F   L   F   P   P   K
    190                                     200
ccc aag gac acc ctc atg atc tcc cgg acc cct gag gtc acg tgc gtg gtg gtg gac gtg  780
 P   K   D   T   L   M   I   S   R   T   P   E   V   T   C   V   V   V   D   V
    210                                     220
agc cac gaa gac ccc gag gtc cag ttc aac tgg tac gtg gac ggc gtg gag gtg cat aat  840
 S   H   E   D   P   E   V   Q   F   N   W   Y   V   D   G   V   E   V   H   N
    230                                     240
gcc aag aca aag cca cgg gag gag cag ttc aac agc acg ttc cgt gtg gtc agc gtc ctc  900
 A   K   T   K   P   R   E   E   Q   F   N   S   T   F   R   V   V   S   V   L
    250                                     260
acc gtt gtg cac cag gac tgg ctg aac ggc aag gag tac aag tgc aag gtc tcc aac aaa  960
 T   V   V   H   Q   D   W   L   N   G   K   E   Y   K   C   K   V   S   N   K
    270                                     280
ggc ctc cca gcc tcc atc gag aaa acc atc tcc aaa acc aaa ggg cag ccc cga gaa cca 1020
 G   L   P   A   S   I   E   K   T   I   S   K   T   K   G   Q   P   R   E   P
    290                                     300
cag gtg tac acc ctg ccc cca tcc cgg gag gag atg acc aag aac cag gtc agc ctg acc 1080
 Q   V   Y   T   L   P   P   S   R   E   E   M   T   K   N   Q   V   S   L   T
    310                                     320
tgc ctg gtc aaa ggc ttc tac ccc agc gac atc gcc gtg gag tgg gag agc aat ggg cag 1140
 C   L   V   K   G   F   Y   P   S   D   I   A   V   E   W   E   S   N   G   Q
    330                                     340
ccg gag aac aac tac aag acc aca cct ccc atg ctg gac tcc gac ggc tcc ttc ttc ctc 1200
 P   E   N   N   Y   K   T   T   P   P   M   L   D   S   D   G   S   F   F   L
    350                                     360
tac agc aag ctc acc gtg gac aag agc agg tgg cag cag ggg aac gtc ttc tca tgc tcc 1260
 Y   S   K   L   T   V   D   K   S   R   W   Q   Q   G   N   V   F   S   C   S
    370                                     380
gtg atg cat gag gct ctg cac aac cac tac acg cag aag agc ctc tcc ctg tct ccg ggt 1320
```

```
 V   M   H   E   A   L   H   N   H   Y   T   Q   K   S   L   S   L   S   P   G
     390                                       400
aaa tga gaa ttc                                                             1332
 K       EcoRI
409
```

Figure 2B. DNA and deduced amino acid sequences of HuEPO-L-vFc$_{\gamma 4}$

DNA Sequence SEQ ID NO: 19

Amino Acid Sequence SEQ ID NO: 20

```
aag ctt ggc gcg gag atg ggg gtg cac gaa tgt cct gcc tgg ctg tgg ctt ctc ctg tcc  60
HindIII              M   G   V   H   E   C   P   A   W   L   W   L   L   L   S
                    -27                                 -20
ctg ctg tcg ctc cct ctg ggc ctc cca gtc ctg ggc gcc cca cca cgc ctc atc tgt gac  120
 L   L   S   L   P   L   G   L   P   V   L   G   A   P   P   R   L   I   C   D
        -10                                     -1   1
agc cga gtc ctg gag agg tac ctc ttg gag gcc aag gag gcc gag aat atc acg acg ggc  180
 S   R   V   L   E   R   Y   L   L   E   A   K   E   A   E   N   I   T   T   G
    10                                      20
tgt gct gaa cac tgc agc ttg aat gag aat atc act gtc cca gac acc aaa gtt aat ttc  240
 C   A   E   H   C   S   L   N   E   N   I   T   V   P   D   T   K   V   N   F
    30                                      40
tat gcc tgg aag agg atg gag gtc ggg cag cag gcc gta gaa gtc tgg cag ggc ctg gcc  300
 Y   A   W   K   R   M   E   V   G   Q   Q   A   V   E   V   W   Q   G   L   A
    50                                      60
ctg ctg tcg gaa gct gtc ctg cgg ggc cag gcc ctg ttg gtc aac tct tcc cag ccg tgg  360
 L   L   S   E   A   V   L   R   G   Q   A   L   L   V   N   S   S   Q   P   W
    70                                      80
gag ccc ctg cag ctg cat gtg gat aaa gcc gtc agt ggc ctt cgc agc ctc acc act ctg  420
 E   P   L   Q   L   H   V   D   K   A   V   S   G   L   R   S   L   T   T   L
    90                                      100
ctt cgg gct ctg gga gcc cag aag gaa gcc atc tcc cct cca gat gcg gcc tca gct gct  480
 L   R   A   L   G   A   Q   K   E   A   I   S   P   P   D   A   A   S   A   A
    110                                     120
cca ctc cga aca atc act gct gac act ttc cgc aaa ctc ttc cga gtc tac tcc aat ttc  540
 P   L   R   T   I   T   A   D   T   F   R   K   L   F   R   V   Y   S   N   F
    130                                     140
ctc cgg gga aag ctg aag ctg tac aca ggg gag gcc tgc agg aca ggg gac gga tcc ggt  600
 L   R   G   K   L   K   L   Y   T   G   E   A   C   R   T   G   D   G   S   G
    150                                     160
ggc ggt tcc ggt gga ggc gga agc ggc ggt gga gga tca gag tcc aaa tat ggt ccc cca  660
 G   G   S   G   G   G   G   S   G   G   G   G   S   E   S   K   Y   G   P   P
    170                                     180
tgc cca cca tgc cca gca cct gag ttc gcg ggg gga cca tca gtc ttc ctg ttc ccc cca  720
 C   P   P   C   P   A   P   E   F   A   G   G   P   S   V   F   L   F   P   P
    190                                     200
aaa ccc aag gac act ctc atg atc tcc cgg acc cct gag gtc acg tgc gtg gtg gtg gac  780
 K   P   K   D   T   L   M   I   S   R   T   P   E   V   T   C   V   V   V   D
    210                                     220
gtg agc cag gaa gac ccc gag gtc cag ttc aac tgg tac gtg gat ggc gtg gag gtg cat  840
 V   S   Q   E   D   P   E   V   Q   F   N   W   Y   V   D   G   V   E   V   H
    230                                     240
aat gcc aag aca aag ccg cgg gag gag cag ttc aac agc acg tac cgt gtg gtc agc gtc  900
 N   A   K   T   K   P   R   E   E   Q   F   N   S   T   Y   R   V   V   S   V
    250                                     260
ctc acc gtc ctg cac cag gac tgg ctg aac ggc aag gag tac aag tgc aag gtc tcc aac  960
 L   T   V   L   H   Q   D   W   L   N   G   K   E   Y   K   C   K   V   S   N
    270                                     280
aaa ggc ctc ccg tcc tcc atc gag aaa acc atc tcc aaa gcc aaa ggg cag ccc cga gag 1020
 K   G   L   P   S   S   I   E   K   T   I   S   K   A   K   G   Q   P   R   E
    290                                     300
cca cag gtg tac acc ctg ccc cca tcc cag gag gag atg acc aag aac cag gtc agc ctg 1080
 P   Q   V   Y   T   L   P   P   S   Q   E   E   M   T   K   N   Q   V   S   L
    310                                     320
acc tgc ctg gtc aaa ggc ttc tac ccc agc gac atc gcc gtg gag tgg gag agc aat ggg 1140
 T   C   L   V   K   G   F   Y   P   S   D   I   A   V   E   W   E   S   N   G
    330                                     340
cag ccg gag aac aac tac aag acc acg cct ccc gtg ctg gac tcc gac ggc tcc ttc ttc 1200
 Q   P   E   N   N   Y   K   T   T   P   P   V   L   D   S   D   G   S   F   F
    350                                     360
ctc tac agc agg cta acc gtg gac aag agc agg tgg cag gag ggg aat gtc ttc tca tgc 1260
 L   Y   S   R   L   T   V   D   K   S   R   W   Q   E   G   N   V   F   S   C
    370                                     380
tcc gtg atg cat gag gct ctg cac aac cac tac aca cag aag agc ctc tcc ctg tct ctg 1320
```

```
 S   V   M   H   E   A   L   H   N   H   Y   T   Q   K   S   L   S   L   S   L
     390                                       400
ggt aaa tga gaa ttc                                                           1335
 G   K       EcoRI
     410
```

Figure 2C. DNA and deduced amino acid sequences of HuEPO-L-vFc$_{\gamma 1}$

DNA Sequence SEQ ID NO: 21

Amino Acid Sequence SEQ ID NO: 22

```
aag ctt ggc gcg gag atg ggg gtg cac gaa tgt cct gcc tgg ctg tgg ctt ctc ctg tcc  60
HindIII          M   G   V   H   E   C   P   A   W   L   W   L   L   L   S
                -27                                 -20
ctg ctg tcg ctc cct ctg ggc ctc cca gtc ctg ggc gcc cca cca cgc ctc atc tgt gac  120
 L   L   S   L   P   L   G   L   P   V   L   G   A   P   P   R   L   I   C   D
        -10                                     -1   1
agc cga gtc ctg gag agg tac ctc ttg gag gcc aag gag gcc gag aat atc acg acg ggc  180
 S   R   V   L   E   R   Y   L   L   E   A   K   E   A   E   N   I   T   T   G
    10                                      20
tgt gct gaa cac tgc agc ttg aat gag aat atc act gtc cca gac acc aaa gtt aat ttc  240
 C   A   E   H   C   S   L   N   E   N   I   T   V   P   D   T   K   V   N   F
    30                                      40
tat gcc tgg aag agg atg gag gtc ggg cag cag gcc gta gaa gtc tgg cag ggc ctg gcc  300
 Y   A   W   K   R   M   E   V   G   Q   Q   A   V   E   V   W   Q   G   L   A
    50                                      60
ctg ctg tcg gaa gct gtc ctg cgg ggc cag gcc ctg ttg gtc aac tct tcc cag ccg tgg  360
 L   L   S   E   A   V   L   R   G   Q   A   L   L   V   N   S   S   Q   P   W
    70                                      80
gag ccc ctg cag ctg cat gtg gat aaa gcc gtc agt ggc ctt cgc agc ctc acc act ctg  420
 E   P   L   Q   L   H   V   D   K   A   V   S   G   L   R   S   L   T   T   L
    90                                      100
ctt cgg gct ctg gga gcc cag aag gaa gcc atc tcc cct cca gat gcg gcc tca gct gct  480
 L   R   A   L   G   A   Q   K   E   A   I   S   P   P   D   A   A   S   A   A
    110                                     120
cca ctc cga aca atc act gct gac act ttc cgc aaa ctc ttc cga gtc tac tcc aat ttc  540
 P   L   R   T   I   T   A   D   T   F   R   K   L   F   R   V   Y   S   N   F
    130                                     140
ctc cgg gga aag ctg aag ctg tac aca ggg gag gcc tgc agg aca ggg gac gga tcc ggt  600
 L   R   G   K   L   K   L   Y   T   G   E   A   C   R   T   G   D   G   S   G
    150                                     160
ggc ggt tcc ggt gga ggc gga agc ggc ggt gga gga tca gac aaa act cac aca tgc cca  660
 G   G   S   G   G   G   G   S   G   G   G   G   S   D   K   T   H   T   C   P
    170                                     180
ccg tgc cca gca cct gaa gtc gcg ggg gga ccg tca gtc ttc ctc ttc ccc cca aaa ccc  720
 P   C   P   A   P   E   V   A   G   G   P   S   V   F   L   F   P   P   K   P
    190                                     200
aag gac acc ctc atg atc tcc cgg aca cct gag gtc aca tgc gtg gtg gtg gac gtg agc  780
 K   D   T   L   M   I   S   R   T   P   E   V   T   C   V   V   V   D   V   S
    210                                     220
cac gaa gac cct gag gtc aag ttc aac tgg tac gtg gac ggc gtg gag gtg cat aat gcc  840
 H   E   D   P   E   V   K   F   N   W   Y   V   D   G   V   E   V   H   N   A
    230                                     240
aag aca aag ccg cgg gag gag cag tac aac agc acg tac cgg gtg gtc agc gtc ctc acc  900
 K   T   K   P   R   E   E   Q   Y   N   S   T   Y   R   V   V   S   V   L   T
    250                                     260
gtc ctg cac cag gac tgg ctg aat ggc aag gag tac aag tgc aag gtc tcc aac aaa gcc  960
 V   L   H   Q   D   W   L   N   G   K   E   Y   K   C   K   V   S   N   K   A
    270                                     280
ctc cca gcc tcc atc gag aaa acc atc tcc aaa gcc aaa ggg cag ccc cga gaa cca cag 1020
 L   P   A   S   I   E   K   T   I   S   K   A   K   G   Q   P   R   E   P   Q
    290                                     300
gtg tac acc ctg ccc cca tcc cgg gat gag ctg acc aag aac cag gtc agc ctg acc tgc 1080
 V   Y   T   L   P   P   S   R   D   E   L   T   K   N   Q   V   S   L   T   C
    310                                     320
ctg gtc aaa ggc ttc tat ccc agc gac atc gcc gtg gag tgg gag agc aat ggg cag ccg 1140
 L   V   K   G   F   Y   P   S   D   I   A   V   E   W   E   S   N   G   Q   P
    330                                     340
gag aac aac tac aag acc acg cct ccc gtg ctg gac tcc gac ggc tcc ttc ttc ctc tac 1200
 E   N   N   Y   K   T   T   P   P   V   L   D   S   D   G   S   F   F   L   Y
    350                                     360
agc aag ctc acc gtg gac aag agc agg tgg cag cag ggg aac gtc ttc tca tgc tcc gtg 1260
 S   K   L   T   V   D   K   S   R   W   Q   Q   G   N   V   F   S   C   S   V
    370                                     380
atg cat gag gct ctg cac aac cac tac acg cag aag agc ctc tcc ctg tct ccg ggt aaa 1320
```

```
M   H   E   A   L   H   N   H   Y   T   Q   K   S   L   S   L   S   P   G   K
    390                                     400
tga gaa ttc                                                                 1329
    EcoRI
```

Figure 3. Effect of HuEPO-L-vFc$_{\gamma 2}$ or rHuEPO, on the proliferation of 32D1.9 cells.

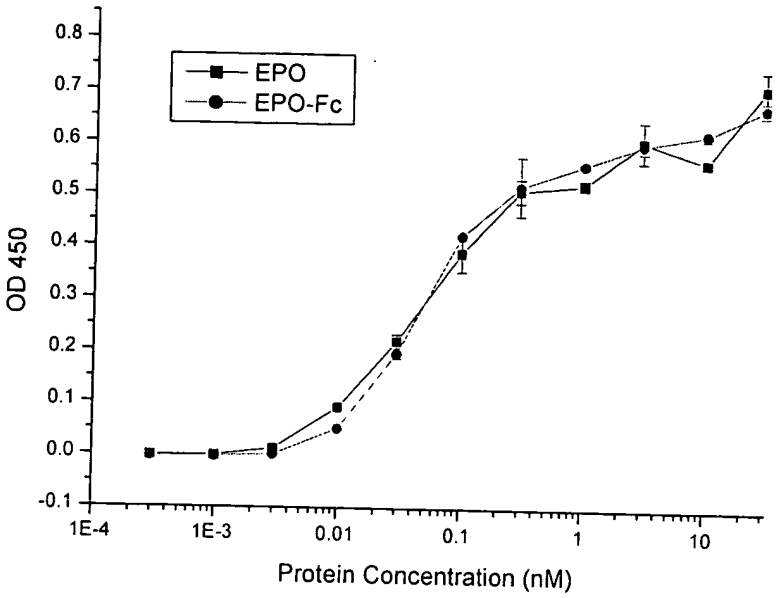

Figure 4. Effect of HuEPO-L-vFc$_{\gamma 2}$ on red blood cell counts in rats.

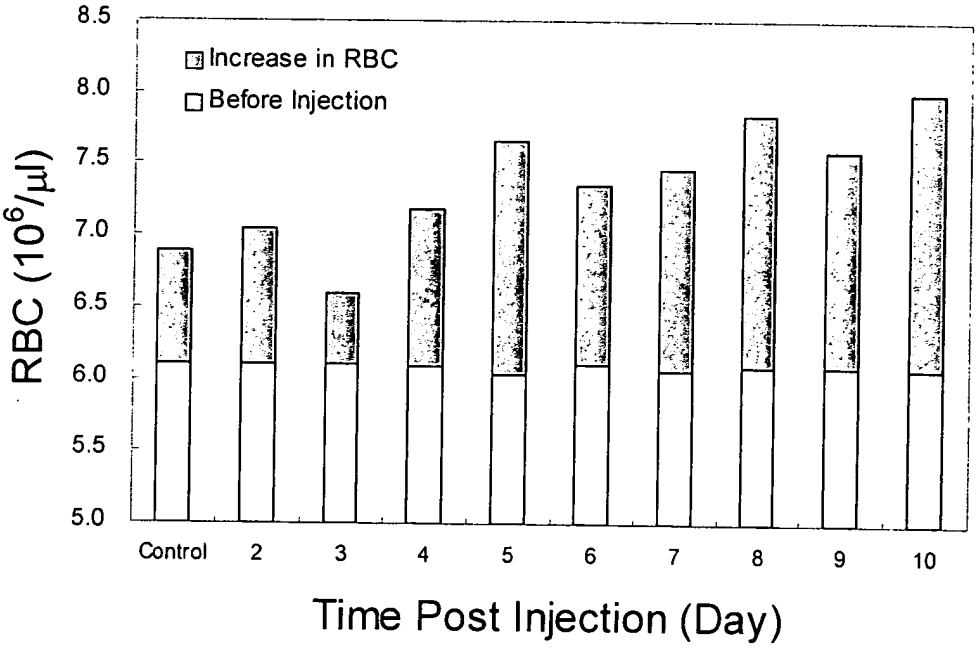

Figure 5. Effect of HuEPO-L-vFc$_{\gamma 2}$ on hemaglobin values in rats.

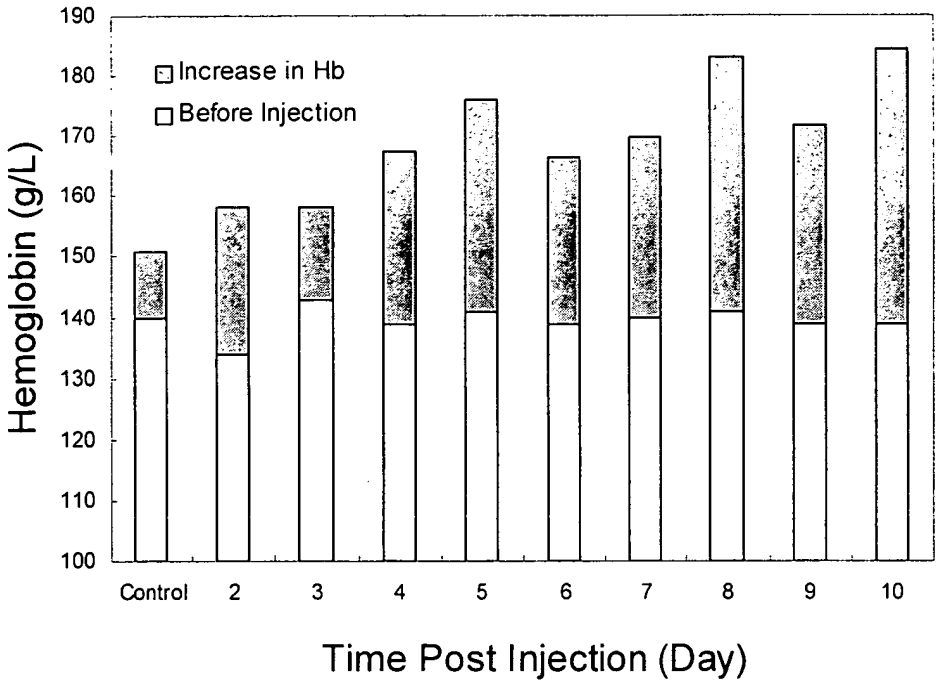

Figure 6. Concentrations of HuEPO-L-vFc$_{\gamma 2}$ in rat serum samples after i.v. injections of the fusion protein.